

## **REMARKS**

### **I. OVERVIEW**

Applicants have reviewed and considered the Office Action mailed August 23, 2006 and the references cited therewith. Claims 1, 7, 25, 45, 57, 69 and 61 have been amended. Support for these amendments may be found throughout the Specification at pages 3, 44, 51, 55-56, 64 and Figure 7. No new matter has been added. Claims 3, 44, 51, 64, 71 and 75 have been canceled. In the Specification, the hyperlinks have been removed. An updated sequence listing including porcine cDNA IGF-1R is submitted with the amendment and requested to be entered. No new matter has been introduced. Applicants believe that they are in compliance with 37 CFR 1.821(d). Upon entry of the foregoing amendments, claims 1-2, 4-43, 45-50, 52-63, 65-70, 72-74 and 76-80 are pending in the instant application. Applicants respectfully request reconsideration of the above-identified application in view of the amendments above and remarks that follow.

### **II. SPECIFICATION**

The Examiner states the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see for example pages 8, 11, 30 and 38. The Examiner requests Applicant to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Accordingly, Applicants have amended the specification to remove embedded hyperlinks at pages 8, 11, 30 and 38 and respectfully request that this objection be withdrawn.

### **III. CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH**

Claims 1-10, 25, 26, 44, 45, 51, 57-64, 71 and 75 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential steps, such omissions amounting to a gap between the steps.

A. The Examiner writes claims 1-10 are drawn to a method for 'genetically identifying an animal with respect to its potential to reproductive longevity', however, there is no method step in which any animal is in fact identified. The Examiner states it is thus unclear how the required method steps actually accomplish the purpose of the method as stated in the preamble of the claim.

Applicants have amended claim 1 so that it now recites in part "identifying that the pig has reproductive longevity potential if the pig has a thymidine at position 3832." Applicants respectfully submit that independent claim 1 is definite and likewise claims 2, and 4-10 dependent on claim 1 are definite. Applicants respectfully request that this rejection be withdrawn and reconsidered.

B. The Examiner writes that claims 25, 26 and 44 are drawn to a method of 'screening animals to determine those more likely to have reproductive longevity', however there is no method step in which a determination is made as to the 'reproductive longevity' of any animal. The Examiner states that it is thus unclear how the required method steps actually accomplish the purpose of the method as stated in the preamble of the claim.

Applicants have amended claim 25 so that it now recites "inferring that the pig is more likely to have reproductive longevity potential if the pig possesses said marker." Applicants respectfully submit that independent claim 25 is definite and likewise claim 26 dependent on

claim 25 is definite. Claim 44 has been canceled. Applicants respectfully request that this rejection be withdrawn and reconsidered.

C. The Examiner writes that claims 45 and 51 are drawn to a method for 'screening animals to determine those more likely to exhibit favorable traits associated with reproductive longevity', however, there is no method step in which a determination is made as to the 'favorable traits associated with reproductive longevity' of any animal. It is thus unclear how the required method steps actually accomplish the purpose of the method as stated in the preamble of the claim.

Applicants have amended claim 45 so that it now recites "inferring that the pig is more likely to exhibit favorable traits if the pig has the allele with a thymidine at position 3832." Applicants respectfully submit that independent claim 45 is definite. Claim 51 has been canceled. Applicants respectfully request that this rejection be withdrawn and reconsidered.

D. The Examiner writes that claims 57-64 are drawn to a method for 'genotyping an animal', however there is no method step in which a determination is made as to the genotype of any animal. It is thus unclear how the required method steps actually accomplish the purpose of the method as stated in the preamble of the claim of 'genotyping an animal' where a genotype is typically described in the art of animal genetics as the nucleic acid content of an organism in both copies of a gene in a diploid organism.

Applicants have amended claim 57 so that it now recites "detecting a polymorphism at position 3832 of SEQ ID NO:23 in both copies of the IGF-1R gene". Applicants respectfully

submit that independent claim 57 is definite and likewise claims 58 -63 dependent on claim 57 are definite. Applicants respectfully request that this rejection be withdrawn and reconsidered.

E. The Examiner writes that claims 71 and 75 are drawn to a method for 'genetically identifying an animal', however there is no method step in which any animal is in fact identified. It is thus unclear how the required method steps actually accomplish the purpose of the method as stated in the preamble of the claim.

While not acquiescing to the Examiner's argument, claims 71 and 75 have been canceled, rendering the basis of this rejection moot.

F. Claims 1-10, 45, 51, and 57-64 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As an initial matter, claims 3, 51 and 64 have been canceled. The Examiner writes that claims 1-10 are unclear over recitation of the phrase 'with respect to its potential to reproductive longevity' in reference to identification of an animal, in claim 1. It is unclear if applicant intends to claim a method that provides indicia of an aspect of 'reproductive longevity', or a method that provides an identification regarding some other quality that may be related to 'reproductive longevity'.

Applicants respectfully disagree. One skilled in the art reviewing the specification, would understand the meaning of this term as used in the claims. However, in order to expedite prosecution, Applicants have amended claim 1 to recite in part "A method for genetically identifying a pig for reproductive longevity potential, wherein the trait of reproductive longevity

potential is characterized by an increase in the number of pregnancies or the duration of time a pig is capable of reproduction relative to the mean of a given population, group or species". In this context, the term conveys the nature of the invention with clarity to the reader and therefore the rejection should be withdrawn.

G. The Examiner writes that claims 45 and 51 are unclear over recitation of the phrase 'favorable traits associated with reproductive longevity' in claim 45. The Examiner states that the term 'favorable' in claim 45 is a relative term which renders the claims indefinite (e.g. one might consider increased longevity favorable for an animal with other phenotypic traits that one is interested in propagating in a population, whereas one might consider increased longevity unfavorable for an animal with other phenotypic traits that one is particularly not interested in propagating in a population. The Examiner writes that the phrase 'favorable traits associated with reproductive longevity' is indefinite because it is not clear if the method screens animals for 'reproductive longevity' or some other trait 'associated with reproductive longevity', thus the metes and bounds of the claim are indefinite.

Applicants disagree. As an initial matter, Applicants have amended claim 45 so that it now recites "wherein the favorable traits of reproductive longevity potential are characterized by an increase in the number of pregnancies or the duration of time a pig is capable of reproduction relative to the mean of a given population, group or species". Support for this amendment can be found throughout the specification, for example, at page 16, lines 24-26. Applicants respectfully remind the Examiner that Applicants are permitted to be their own lexicographer and can define their invention using any phrases that define the patentable subject matter with a reasonable degree of particularity and distinctness. MPEP §§ 2173.01-2173.02. Therefore the phrase

'favorable traits associated with reproductive longevity, wherein the trait of reproductive longevity potential is selected from the group consisting of an increase in the number of pregnancies or the duration of time a pig is capable of reproduction relative to the mean of a given population, group or species' is not indefinite. Furthermore, claims are not analyzed in a vacuum, rather they are analyzed in light of the disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP § 2173.02.

Applicants respectfully submit that if the phrases are definite. Furthermore, if the claims are analyzed in light of the specification the claims are described with a reasonable degree of clarity and particularity as required under MPEP § 2173.02. MPEP § 2173.02 further provides that "Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." If the Examiner maintains that the phrases are indefinite, the Applicants invite the Examiner to suggest alternative, comparable phrases that are supported by the disclosure. In light of the above, Applicants respectfully request that the rejection be withdrawn.

H. The Examiner writes that claims 57-64 are unclear over recitation of the term 'allele 2' in regard to the genotype of an animal as it is allegedly unclear if applicant intends to claim a particular genotype (e.g. specific nucleotide content at a specific position in a particular gene), or what is encompassed by the term 'allele 2'.

Applicants have amended claim 57 to remove the phrase "allele 2". Claim 57 has been amended to recite in part "detecting a polymorphism at position 3832 of SEQ ID NO:23 in both copies of the IGF-1R gene of the pig, wherein a thymidine at position 3832 in both copies of the

IGF-1R gene of SEQ ID NO:23 indicates the pig has reproductive longevity potential." Support for this amendment can be found throughout the specification, for example, at pages 55-56. Applicants respectfully submit that independent claim 57 is definite and likewise claims 58-63 dependent on claim 57 is definite. In light of the above amendment, Applicants respectfully request that this rejection be withdrawn and reconsidered.

I. The Examiner writes that claims 59 and 60 are unclear over recitation of the phrase 'prior to digesting the nucleic acid with a restriction enzyme' in claim 59 because there is no antecedent basis for the digestion of any nucleic acid with a restriction enzyme.

Claim 59 has been amended so that it now depends from claim 58, rather than claim 57. In light of the above amendment, Applicants respectfully request that this rejection be withdrawn and reconsidered.

J. The Examiner writes that claim 61 is unclear over recitation of the phrase 'the restriction enzyme is FokI' because there is no antecedent basis for any restriction enzyme in the claim.

Claim 61 has been amended so that it now depends from claim 58, rather than claim 57. In light of the above amendment, Applicants respectfully request that this rejection be withdrawn and reconsidered.

#### **IV. CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH**

Claims 1-10, 25, 26, 44, 45, 51, 57-64, 71 and 75 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The

Examiner states the claims are broadly drawn to methods comprising the analysis of nucleic acids that are indicative of reproductive longevity and encompass a multitude of different nucleic acid molecules of a wide variety of unique sequences.

The Examiner writes, in the instant application, because of the small amount of structural information regarding nucleic acid polymorphisms in the IGF-1R gene associated with reproductive longevity, one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed by the claimed methods, regardless of the complexity or simplicity of the method of identification.

Applicants respectfully disagree but in order to expedite prosecution, Applicants have amended claims 1, 25, 45, and 57 so that they now require pigs rather than other animals and structurally require a polymorphism at position 3832 of SEQ ID NO:23 in the IGF-1R gene. Support for this amendment can be found throughout the specification, for example, at page 55-56, Figure 7, and in original claims 3, 44, 51, and 64.

In light of the above, Applicants respectfully request that this rejection be withdrawn and reconsidered.

#### **V. CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH -- ENABLEMENT**

Claims 1-10, 25, 26, 44, 45, 51, 57-64, 71 and 75 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Examiner writes while the specification teaches that 'reproductive longevity' means a biologically significant increase in the number of pregnancies and/or the duration of time an animal is capable of reproduction, relative to the mean of a given population, group or species (p.



16), the references does not teach any particular numbers for the parity of the sows used in the example.

Applicants respectfully disagree that one skilled in the art could not make and use the present invention. As an initial matter, independent claims 1, 25, 45, and 57 have been amended to require pigs, to determine a polymorphism at position 3832 in SEQ ID NO:23, where the polymorphism is associated with reproductive longevity potential characterized by an increase in the number of pregnancies or the duration of time a pig is capable of reproduction, relative to the mean of a given population, group or species. Support for these amendments may be found throughout the specification, for example, at pages 55-56, 3, 44, 51, and 64. Although Applicants have not stated an exact number for the increase in pregnancies, Applicants teach at page 55 in the specification, that pigs homozygous for the “2” allele are expected to produce more parities than those that are not pigs homozygous for the “2” allele. Example 3 teaches that the daughters of boars of genotype 12 or 22 have better reproductive longevity than the daughters of boars of the 11 genotype.

The Examiner writes that the specification asserts that there is a positive association between sow homozygosity and reproductive longevity ( $p=0.062$ ), but the specification does not teach that the genotypes of any of the sows in this second study of SNP 3832 was in fact determined.

The Examiner is correct. As is common practice in this field, only the sires were genotyped. However, Applicants disagree with the Examiner's conclusion that the first analysis (using 996 sows) is questionable because of the data structure (p. 55, Lines. 10-11). Applicants assert that while the effects might be overestimated, the p-values are accurate. Although the

expected additive effect is less than or equal to 1.11 parities, the association is still be highly significant ( $P=0.004$ ).

The Examiner states that the data presented for the second analysis (using over 19,000 sows from 179 sires) does not teach consistent and significant correlation of SNP 3832 with reproductive longevity in pigs because it has an association with a p-value of  $P=0.062$ . The Examiner relies on Thisted (1998) for the proposition that an association is statistically significant only if the p-value is less than 0.05.

Applicants respectfully disagree and submit that even though the p-value of the analysis of the SNP3832 data is 0.062, it does not indicate that the association of the SNP with reproductive longevity is inconsistent or insignificant. It is well known that a small sample size, can influence the p-value. Here, Applicants analyzed a small sample size – only 179 sires were genotyped. Furthermore, as noted by Thisted at pages 5-6, having a p-value greater than 0.05 does not mean that the evidence being presented is unconvincing, nor does it indicate that the treatments with a p-value greater than 0.05 are ineffective.

One skilled in the art would be able to make and use the present invention. Enablement requires that one skilled in the art can identify operative embodiments without engaging in undue experimentation. MPEP § 2164.06. "The test is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (*In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Applicants' specification provides ample guidance to the skilled artisan seeking to identify whether a pig is more likely to have reproductive longevity by determining a polymorphism in the IGF-1R gene that is associated with reproductive longevity. Claims 1, 25, 45 and 57 are

directed to methods of identifying, screening or genotyping pigs for reproductive longevity potential. The claims are not directed to the polymorphisms themselves. Applicants submit that given the sequence SEQ ID NO: 23 along with the claims and the teaching in the specification, one of skill in the art would know how to genotype pigs for polymorphisms at position 3832 of SEQ ID NO:23 in the porcine IGF-1R gene associated with reproductive longevity potential characterized by an increase in parity or the duration of time a pig is capable of reproduction, relative to the mean of a given population, group or species.

Thus, claims are enabled. Therefore, one of skill in the art would be able to use the methods of the claimed invention without “undue experimentation”. In light of the above, Applicants submit that the claims are fully enabling and commensurate in scope with the disclosure of the claimed invention. Therefore, Applicants request that the rejections under 35 USC §112 be withdrawn and reconsidered.

## **VI. CLAIM REJECTIONS - 35 U.S.C. § 102**

Claims 1-4, 25, 26, 44, 45, 51, 57, 63, 64, 71, and 75 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Harumi et al (2001 as cited in the IDS). The Examiner relies on Harumi et al. as teaching an analysis of the pig IGF-1R gene sequence using RT-PCR analysis of the cDNA sequence, and the identification of polymorphic positions within the sequence. The Examiner writes that, regarding claim 1, the reference teaches a method comprising obtaining a sample of genetic material from an animal (p. 386, right column, first paragraph), and assaying for the presence of a polymorphism in the IGF-1R gene sequence (p. 388, left col., Fig 2). The Examiner continues, regarding claim 2, the reference teaches the single nucleotide polymorphism at position 3832 (Figure 2). The Examiner writes that if Applicant

asserts that the SNP 3832 is associated with reproductive longevity, then this association is an inherent property of the polymorphism.

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of anticipation because the reference does not teach each and every claim element. Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Dillon* 919 F.2d 688, 16 USPQ2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991). At the outset, claims 3, 44, 51, 64, 71 and 75 have been canceled. Claims 1, 25, 45 and 57 recite methods of identifying, screening or genotyping pigs for reproductive longevity potential. In contrast, Harumi describes the identification of polymorphisms in the porcine IGF-1R gene. Importantly, this reference is silent with respect to the polymorphisms association with any trait. In response to the Examiner's line of reasoning that if SNP 3832 is associated with reproductive longevity, then this association is an inherent property of the polymorphism, Applicants remind the Examiner that the instant claims are not composition of matter claims, for example, to the SNPs themselves. Harumi does not teach or suggest to one skilled in the art that polymorphisms of the porcine IGF-1R gene are associated with reproductive longevity potential. Therefore, Harumi cannot teach methods of identifying or screening pigs for reproductive longevity potential. Moreover, the Court of Appeals for the Federal Circuit recently stated that "If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation." *Elan Pharmaceuticals v. Mayo Foundation for Medical Education and Research* 2002US App. Lexis 26092 (Fed Cir. Dec. 18, 2002). Thus, Harumi does not expressly or inherently anticipate the claimed methods.

In light of the above, Applicants respectfully request that the rejection be withdrawn and reconsidered.

## VII. CLAIM REJECTIONS - 35 U.S.C. § 103

Claim 6 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Harumi et al (2001 as cited in the IDS) in view of Larsen et al. (2001).

The Examiner writes that Harumi et al. teaches a method comprising obtaining a sample of genetic material from an animal (p. 386, right column, first paragraph), and assaying for the presence of a polymorphism in the IGF-1R gene sequence (p. 388, left col., Fig 2). The Examiner states that the reference teaches the detection of the C/T polymorphism at position 3832 and if applicant asserts that the SNP 3832 is associated with reproductive longevity, then this association is an inherent property of the polymorphism.

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness because, even if combined, the cited references fail to teach or suggest all of the elements of Applicants' claimed invention. To support a *prima facie* case of obviousness, the references must provide motivation for one of ordinary skill in the art to practice the claimed invention as well as provide a reasonable expectation of success. For the reasons in the preceding paragraphs, one of ordinary skill in the art at the time of invention could not have had any reasonable expectation in advance that a polymorphism in a porcine IGF-1R gene could be used to identify pigs with reproductive longevity potential.

The Harumi reference shows no correlation of the SNPs with any trait. In this process, it is by no means obvious which trait polymorphisms will be associated with. The mere disclosure in Harumi of polymorphisms in the IGF-1R gene in pigs is at most an invitation to experiment.

Indeed, the reference fails to provide any of the SNPs association with reproductive longevity potential. Thus, Harumi does not teach or suggest to one skilled in the art that all polymorphisms of the IGF-1R gene are associated with reproductive longevity in pigs. Importantly, Applicants are claiming methods of identifying pigs for reproductive longevity, not composition of matter claims to SNPs. Examiner has failed to provide any evidence for a teaching, motivation or suggestion to modify the method of Harumi. Neither Harumi, nor the Laresen reference, would immediately point one of ordinary skill in the art to methods of screening pigs for reproductive longevity using polymorphisms in porcine IGF-1R associated with reproductive longevity as claimed by Applicants. Thus, claim 6 is not obvious and is patentable over Harumi and Larsen et al for the reasons argued above, plus the elements in the claim. Therefore, Applicants respectfully request that the rejection under 35 USC § 103 be withdrawn and reconsidered.

#### **VIII. SEQUENCE LISTING**

Applicants have submitted the updated sequence listing so that it includes porcine IGF-1R cDNA (SEQ ID NO:23) in an electronic version with the sequence listing and statements under 37 CFR 1.821(f) and (g). No new matter has been added. Applicants believe that they are in compliance with 37 C.F.R. § 1.821(d).

#### **IX. CONCLUSION**

In the event that there are any questions relating to this amendment, Applicants invite the Examiner to call the undersigned attorney so that prosecution can be expedited.

Please consider this a one-month extension of time from November 23, 2006 to December 23, 2006 and charge Deposit Account No. 26-0084 the amount of \$120.00 for this

extension. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Janae E. Lehman Bell". The signature is fluid and cursive, with the first name "Janae" being the most prominent.

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